DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

SP 99P-0794/CP 1

NOV 5 1999

Gene Komer, Ph.D.
President
Veterinary Research Associates, Inc.
2817 West County Road 54G
Fort Collins, CO 80524

Dear Dr. Komer:

We refer to your suitability petition filed March 31, 1999, in which you requested permission to submit an abbreviated new animal drug application (ANADA) to provide for the use of a generic propofol injection. The proposed generic differs in strength, dosage form, and inactive ingredients from the pioneer product, PropoFlo™ (NADA 141-098), which was approved for Abbott Laboratories in 1998.

Strength. The proposed generic product contains 25 mg/mL propofol whereas the pioneer product contains 10 mg/mL propofol.

Dosage form. The propofol in the proposed generic product is a clear solution, whereas the pioneer product is an emulsion.

Inactive ingredients. The inactive ingredients of the proposed generic product are different from those of the pioneer, including the addition of an innovative inactive ingredient, N-methyl-pyrrolidone, which has not been previously approved in an IV drug product for dogs.

Changes in dosage form and strength are variances from the pioneer product that can be considered through a suitability petition, under section 512(n)(3) of the Federal Food Drug, and Cosmetic Act (FFDCA). However, the Center for Veterinary Medicine has identified the proposed changes as changes that may adversely affect the product's safety and/or effectiveness.

The proposed generic contains 25 mg/mL propofol for IV use in dogs, whereas the pioneer product contains 10 mg/mL propofol for IV use in dogs – more than a twofold difference. The labeling for the pioneer product states that propofol is intended for induction and maintenance of general anesthesia in dogs. The labeling for the pioneer shows that induction dose ranges are narrow (5.5-7.0 mg/kg body weight) and dosage rates are critically dependant on volume (0.37 – 0.70 mL/kg per minute) for dogs given propofol alone. The labeling cautions that rapid administration or accidental overdosage may cause neurologic and cardiopulmonary depression, and that respiratory arrest may occur. If the product is injected too slowly, an inadequate plane of anesthesia can occur. In view of the above safety concerns relating to change of strength, especially when such change occurs in conjunction

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with different inactive ingredients, including the addition of an innovative inactive ingredient, the Center has determined that studies other than bioequivalence will be required to show the safety and/or effectiveness of propofol injection for induction and maintenance of anesthesia.

Section 512(n)(3)(C) of the FFDCA provides for suitability petitions to be denied if investigations must be conducted to show the safety and effectiveness, in animals to be treated with the drug, of the strength of the proposed product when it differs from the strength of the approved new animal drug.

Because investigations beyond bioequivalence are required for approval of your proposed product, the suitability petition is denied. Hence, the product is ineligible for consideration under an ANADA. A New Animal Drug Application (NADA) would be required to obtain approval of your proposed product.

If you disagree with our denial of your suitability petition, you may petition for reconsideration of the denial following the procedures set forth in 21 CFR 10.33. Such a petition must be based solely on the information and views contained in your original petition and must be submitted in accordance with § 10.20 in the format outlined in § 10.33. The petition for reconsideration must be submitted no later than 30 days after the date of this denial of the suitability petition, and should be filed with the Dockets Management Branch, Food and Drug Administration, HFA-305, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Please refer to the docket number cited above in any submission regarding this original suitability petition.

If there is additional information, not included as part of your original submission, that you would like the agency to consider, you should submit a new petition including all the necessary information to the Dockets Management Branch, at the address noted above.

If you have additional questions about the specific requirements for the NADA, please contact Dr. Melanie Berson, Director, Division of Therapeutic Drugs for Non-Food Animals (HFV-110), telephone (301) 827-7540.

Sincerely yours,

Claire M. Lathers

Claire M. Lathers, Ph.D., F.C.P.
Director
Office of New Animal Drug Evaluation
Center for Veterinary Medicine

11/5/99